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Please find below and/or attached an Office communication concerning this application or proceeding.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/696,909
Filing Date: October 29, 2003
Appellant(s): LORENS ET AL.

Susan W. Graf
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed November 21, 2008 appealing from the Office action mailed June 23, 2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows:

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner. The rejection of Claims 1, 12, 14-18, 27, 41-44 and 55-61 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, set forth in section 4-pages 2-9 of the Office Action of 6/23/2008 and the rejection of claims 1, 12, and 14-18 under 35 U.S.C. 112, second paragraph, set forth in section 5-page 9 of the Office Action of 6/23/208.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

1. Healy et al. (Am. J. of Physiology, Lung Cell Molecular Physiology, June, 2001 280: L1273-L1281).

2. Varner and Cheresh (Current Opinion in Cell Biology, October 1996, 8:724-730).

3. US Patent No. 6,180,084 (Ruoslahti et al. January, 2001).

4. US Patent Application Publication No.: 2004/0048253 (Panzer et al. February 21, 2001).

5. US Patent Application Publication No.: 2004/0077574 (Klinghoffer et al., May 23, 2002).

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. The rejection of claims 1, 14, 27, 54-56 and 61 under 35 U.S.C. 102(b) as being anticipated by Healy et al. (Am. J. of Physiology, Lung Cell Molecular Physiology, June, 2001 280: L1273-L1281) is maintained for the reasons of record.

Healy et al. teaches determining the in vitro kinase activity of an Axl polypeptide where the Axl polypeptide has kinase activity in the absence of the compound, see Fig. 5 and page L1276, 2nd col. Healy et al. teaches performing a cell-based assay in an endothelial cell by contacting human pulmonary endothelial cells that express human Axl (see Fig. 2) with the Axl ligand Gas 6 and determining the effect of this interaction on cell number, see Abstract, p. 1276, left column, and Fig. 6. Healy et al. teaches assaying apoptosis in human endothelial cells expressing recombinant wild type Axl, see p. L1278 and Figure 9 and 10.

It is noted that the specification teaches assaying increases or decreases in cellular proliferation and apoptosis as cell based assays for assaying the effect of the test compounds and are among the "functional effects" contemplated for assaying the potential inhibitor, see page 8, line 15-to page 9, line 5. Thus "determining the functional effects of the compound upon the kinase activity of the Axl polypeptide", when given its broadest reasonable interpretation, encompasses assaying cellular responses such as increases or decreases in cellular proliferation and apoptosis

It is noted that a wherein clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited, MPEP 2111.04. Given that the method of the prior art comprises the same method steps as claimed in the instant invention, determining, *in vitro* kinase activity of an Axl polypeptide comprising an amino acid sequence with greater than 95% identity to full length SEQ ID NO: 4, wherein the Axl polypeptide has kinase activity in the absence of said compound; and performing a cell based assay in an endothelial cell comprising said Axl polypeptide, which assay produces an angiogenesis phenotype in said endothelial cell in the absence of the compound, the claimed method is

anticipated because the method will inherently be a method for identifying a compound that inhibits angiogenesis, wherein inhibition of the in vitro kinase activity of the Axl polypeptide in the presence of the compound and inhibition of the angiogenesis phenotype in the cell-based assay in the presence of the compound identifies the compound as a compound that inhibits angiogenesis, wherein inhibition of the angiogenesis phenotype in the cell-based assay in the presence of the compound identifies the compound as a compound that inhibits angiogenesis, wherein inhibition of the angiogenesis phenotype in the cell-based assay is caused by down regulation of expression of the Axl polypeptide, or wherein inhibition of the kinase activity of the Axl polypeptide in the presence of the compound identifies the compound as a compound that inhibits angiogenesis. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993). Although the reference does not specifically state that the method is a method for identifying a compound that inhibits angiogenesis, the claimed method appears to be the same as the prior art method, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the method of the prior art does not possess the same material, structural and functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed method is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA).

Although the reference does not specifically that the Axl of the reference is SEQ ID NO: 4 given that the Axl polypeptide of SEQ ID NO: 4 and Healy et al. are human Axl, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence

needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from that taught by the prior art and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977).

Claim Rejections - 35 USC § 103

7. The rejection of claims 12, 15-18, 41-44, and 57-60 under 35 U.S.C. 103(a) as being unpatentable over Healy et al. (Am. J. of Physiology, Lung Cell Molecular Physiology, June, 2001 280: L1273-L1281) as applied to claims 1, 14, 27, 54-56 and 61, above, in view of Varner and Cheresh (Current Opinion in Cell Biology, October 1996, 8:724-730) in further view of US Patent No. 6,180,084 (Ruoslahti et al. January, 2001), in further view of US Patent Application Publication No.: 2004/0048253 (Panzer et al. February 21, 2001)), and in further view of US Patent Application Publication No.: 2004/0077574 (Klinghoffer et al., May 23, 2002) is being maintained for the reasons of record.

Healy et al. teach as described *supra*.

Healy et al. do not teach determining the functional effect by measuring $\alpha V\beta 3$ expression or haptotaxis or the use of an antibody, an antisense molecule, an RNAi molecule, or a small organic molecule.

Varner and Cheresh teach that integrin $\alpha V\beta 3$ is significantly upregulated on vascular cells within human tumors and in response to growth factors and plays a biological role in a

critical event of blood vessel formation during tumor angiogenesis, see section on Role of Integrins in Tumor Angiogenesis, p. 726- 727.

Panzer et al. teach the common art practice of screening small molecules, antibodies, oligonucleotides, and the antisense molecules for use in diagnosis and therapies, see para 0735-0741 and 0754-0757of the published application. Similarly Ruoslahti et al teach the common art practice of screening organic chemicals, nucleic acid molecules such as RNA, a cDNA, or oligonucleotides, and antibodies for use in therapies, see Col 1, 2, 9-12.

Klinghoffer et al. teach that siRNA polynucleotides offer advantages over other types of polynucleotides for sequence specific alteration of gene expression including lower effective siRNA polynucleotide concentration, enhance stability, shorter lengths, they are readily taken up by intact cells, and are effective at concentration that are several orders of magnitude lower than those required for either antisense or ribozyme polynucleotides, see paragraph 0025.

It would have been *prima facie* obvious at the time the invention was made to perform the method of claim 1 by measuring $\alpha V\beta 3$ expression and to use an antibody, antisense molecule, RNAi, or small organic molecule as the compound to use in the screening methods for claims 1, 27, and 56 because the level $\alpha V\beta 3$ expression was known to be important in angiogenesis and the screening of various modulatory compounds for therapeutic purposes was conventionally used in the art at the time of the invention and the advantages of siRNA over other sequence specific modulators was well known in the art at the time the invention was made. Thus one of ordinary skill in the art would have had motivation and a reasonable expectation of success in making and using the claimed invention.

(10) Response to Argument

Claim Rejections - 35 USC § 102

Rejection of claims 1, 14, 54, and 55

Appellant argues that the Office alleges that Healy et al. teach "determining the in vitro kinase activity of an Axl polypeptide... [,] performing a cell-based assay in an endothelial cell.., and determining the effect of this interaction on cell number..." as well as teaching assaying apoptosis in endothelial cells expressing Axl (Office action of June 23, 2008, page 10, second paragraph). Appellant argues that the Office further asserts that as Healy allegedly "comprises the same method steps as claimed in the instant invention, determining in vitro kinase activity of an Axl polypeptide...; and performing a cell based assay in an endothelial cell comprising said Axl polypeptide.., the claimed method is anticipated because the method will inherently be a method for identifying a compound that inhibits angiogenesis..." (Office action, paragraph bridging pages 10-11, emphasis added).

Appellant argues that a rejection under 35 U.S.C. § 102 is appropriate "only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference." MPEP § 2131. Further, "the prior art reference - in order to anticipate under 35 U.S.C. § 102 - must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements 'arranged as in the claim.'" *Net MoneyIN, Inc. v. Verisign Inc.* Fed. Cir., Appeal No. 2007-1565, October 20, 2008, emphasis added.

Appellant argues that importantly, Healy et al. do not teach the combination of assaying in vitro kinase activity of an Axl polypeptide in the presence of a test compound and performing a cell-based assay in the presence of the compound which produces an angiogenesis phenotype in the absence of the test compound, as in claim 1. In order to anticipate the claims, the reference

must disclose the limitations arranged as they are in the claim. This "refers to the need for an anticipatory reference to show all of the limitations of the claims *arranged or combined* in the same way as recited in the claims..." *NetMoneyIN, Inc. v. Verisign Inc.* Fed. Cir., Appeal No. 2007-1565, October 20, 2008, emphasis added. Appellant argues that in order for Healy et al. to anticipate claim 1, it must teach the combination of assays as it is found in Appellant's claim. Appellant argues that however, while Healy et al. describe that contacting human pulmonary artery endothelial cells (HPAEC), which express Axl polypeptide, with exogenous Gas 6 (an Axl ligand) increased Axl phosphorylation (page L1276, column 2 and Figure 5), increased cell number (page L1276, column 2 and Figure 6), and decreased apoptosis of the cells in serum free medium (page L1277, column 2; page 1278, column 2; Figures 8 and 10), these assays are all described independently. Nowhere, does Healy et al. describe combining these assays, let alone that these assays would identify or could be used to identify an inhibitor of angiogenesis. Thus, Healy et al. does not anticipate claim 1 or dependent claims 14, 54, and 55.

Appellant's arguments have been considered, but have not been found persuasive because claim 1 and its dependent claims have no limitations on the order or arrangement in which the steps are performed. In regard to *Net MoneyIN, Inc. v. Verisign Inc.* Fed. Cir., Appeal No. 2007-1565, October 20, 2008, claim 23 of US Pat. No. 5,822,737 patent reviewed for anticipation specifically denotes steps a)-e) in the claim and the steps are drawn to five different links between different aspects of the invention. Thus, given that claim 1 does not have such limitations on the order or arrangement in which the steps are to be performed and can reasonably be interpreted to be performed in any order, Appellant's arguments are not found persuasive.

Appellant argues that further, Healy et al. do not teach that Gas 6 (an Axl polypeptide agonist) is an angiogenesis inhibitor. Appellant argues that this has been previously noted by Applicants (Office action response of February 23, 2007, page 15, third paragraph). This has also been *admitted by the Office*, which stated "Healy does not teach that Gas 6 specifically inhibits angiogenesis..." (Office action of May 7, 2007, page 11, third paragraph). Further, Healy et al. do not teach contacting Axl or cells comprising Axl with any compound other than Gas 6. In the Office action of May 7, 2007, the Office attempted to cure the deficiencies of Healy et al. by asserting that Gallicchio et al. (Blood 105:1970-1976, 2005; cited in the Office action of May 7, 2007) provides evidence that Gas 6 inhibits angiogenesis upon interacting with Axl (Office action of May 7, 2007, page 12, first paragraph), and that Healy et al. thus inherently anticipates Appellant's claims. Appellant argues that Gallicchio et al. does not provide evidence that Healy et al. inherently anticipates claims 1, 14, 54, and 55.

Appellant argues that "The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic ... Inherency, however, may not be established by probabilities or possibilities." MPEP § 2112. To show inherency, a gap in a reference may be filled by extrinsic evidence, but the "evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991); MPEP§ 2131.01, emphasis added. Appellant argues that Healy et al. does not expressly anticipate the claimed methods, nor has the Office has not provided any extrinsic evidence to make it clear that Healy et al. necessarily inherently anticipates the claims. Instead, Gallicchio et al., the only

evidence proffered by the Office, makes it clear that Healy et al. do not anticipate any of the present claims.

Appellant argues that based on Gallicchio et al., one of skill in the art would predict that inhibition of Axl polypeptide activity would stimulate activation of an angiogenic program in vascular endothelial cells. Gas 6 stimulates Axl polypeptide activity, which inhibits activation of vascular endothelial growth factor receptor 2 (VEGFR2) and leads to inhibition of an angiogenic program in vascular endothelial cells (Gallicchio et al., abstract; page 1973, first full paragraph; Figure 4A). Appellant argues that, based on Gallicchio et al., one of skill in the art would predict that inhibition of Axl would activate VEGFR2 and lead to stimulation of angiogenesis. Thus, the expected effect of Healy et al. would be the opposite of Appellant's demonstrated inhibition of angiogenesis by inhibition of Axl. Appellant argues that as Gas 6 is not an inhibitor of Axl, Healy et al. do not expressly or inherently teach the claimed method for identifying a compound that is an inhibitor of angiogenesis and therefore this reference does not anticipate any of the claims (including independent claims 1, 27, and 56 and any claims that depend from these claims).

Appellant argues that that the foregoing discussion was previously presented in the amendment of October 5, 2007 and it was tacitly acknowledged and accepted as persuasive by the Office, which withdrew this rejection (of all claims) without comment in the Office action of December 12, 2007. Appellant argues that this rejection under 35 U.S.C. § 102(b) has previously been overcome and that Healy et al. still does not anticipate the claims.

Appellant's arguments have been considered, but have not been found persuasive because the recitation of identifying a compound that inhibits angiogenesis has not been given patentable

weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). Additionally, it is noted that a wherein clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited, MPEP 2111.04. Given that Healy et al. teach determining the *in vitro* kinase activity of an Axl polypeptide where the Axl polypeptide has kinase activity in the absence of the compound, (see Fig. 5 and page L1276, 2nd col.), performing a cell-based assay in an endothelial cell by contacting human pulmonary endothelial cells that express human Axl (see Fig. 2) with the Axl ligand Gas 6 and determining the effect of this interaction on cell number (see Abstract, p. 1276, left column, and Fig. 6), and assaying apoptosis in human endothelial cells expressing recombinant wild type Axl (see p. L1278 and Figure 9 and 10), the limitations of the claimed process steps are met. The claims do not limit the compound to be tested. Thus, regardless of wheter or not Gallichio et al.(which was not relied upon in the instant rejection) teach that GAS-6 inhibits angiogenesis, GAS-6 meets the limitations of a compound to be used in the claimed method. Based on the teachings of Healy et al. one of skill in the art would immediately envision that the desribed assays could be used for determining positive or negative effects of a compound on the endothelial cells and Axl activity.

Rejection of claims 27 and 54

Appellant argues that the Office alleges that Healy et al. teach "determining the in vitro kinase activity of an Axl polypeptide... [,] performing a cell-based assay in an endothelial cell.., and determining the effect of this interaction on cell number..." as well as teaching assaying apoptosis in endothelial cells expressing Axl (Office action of June 23, 2008, page 10, second paragraph). Appellant argues that the Office further asserts that as Healy allegedly "comprises the same method steps as claimed in the instant invention, determining in vitro kinase activity of an Axl polypeptide...; and performing a cell based assay in an endothelial cell comprising said Axl polypeptide.., the claimed method is anticipated because the method will inherently be a method for identifying a compound that inhibits angiogenesis..." (Office action, paragraph bridging pages 10-11, emphasis added).

Appellant argues that Healy et al. do not teach that Gas 6 (an Axl polypeptide agonist) is an angiogenesis inhibitor. Appellant argues that this has been previously noted by Appellants (Office action response of February 23, 2007, page 15, third paragraph, and above). Appellant argues that this has also been *admitted by the Office*, which stated "Healy does not teach that Gas 6 specifically inhibits angiogenesis..." (Office action of May 7, 2007, page 11, third paragraph). Further, Healy et al. do not teach contacting Axl or cells comprising Axl with any compound other than Gas 6. In the Office action of May 7, 2007, the Office attempted to cure the deficiencies of Healy et al. by asserting that Gallicchio et al. (Blood 105:1970-1976, 2005; cited in the Office action of May 7, 2007) provides evidence that Gas 6 inhibits angiogenesis upon interacting with Axl (Office action of May 7, 2007, page 12, first paragraph) and that Healy et al. thus inherently anticipates Applicants' claims.

Appellant argues that as discussed above, based on Gallicchio et al., one of skill in the art would predict that inhibition of Axl polypeptide activity would stimulate activation of an angiogenic program in vascular endothelial cells. Gas 6 stimulates Axl polypeptide activity, which inhibits activation of vascular endothelial growth factor receptor 2 (VEGFR2) and leads to inhibition of an angiogenic program in vascular endothelial cells (Gallicchio et al., abstract; page 1973, first full paragraph; Figure 4A). Appellant argues that therefore, based on Gallicchio et al., one of skill in the art would predict that inhibition of Axl would activate VEGFR2 and lead to stimulation of angiogenesis. Appellant argues that thus, the expected effect of Healy et al. would be the opposite of Appellant's demonstrated inhibition of angiogenesis. Appellant argues that as Gas 6 is not an inhibitor of Axl, Healy et al. do not expressly or inherently teach the claimed method of identifying a compound that is an inhibitor of angiogenesis and therefore this reference does not anticipate any of the claims (including independent claims 1, 27, and 56 and any claims that depend from these claims).

Appellant's arguments have been considered, but have not been found persuasive because the preamble and the wherein clause expressing the intended result of a process step positively recited were not given patentable weight for comparison of the claims with the prior art, for the reasons set forth above. Additionally, the claims do not have any limitation on the compound to be used in the claimed methods of identification of compouns that inhibit angiogenesi, thus GAS6 meets the limitations of the claims. Thus, regardless of wheter or not Gallichio et al.(which was not relied upon in the instant rejection) teach that GAS-6 inhibits angiogenesis, GAS-6 meets the limitations of a compound to be used in the claimed method. Thus, given that Healy et al. teach contacting cells comprising recombinant Axl polypeptide with GAS-6 and

performing a cell-based assay, which assay produces an angiogensis phenotype in said endothelial cell in the absence of the compound, claims 27 and 54 are anticipated for the reasons previously set forth and above.

Rejection of claims 56 and 61

Appellant argues that the Office states that "'determining the functional effects of the compound upon the kinase activity of the Axl polypeptide,' when given its broadest reasonable interpretation encompasses assaying cellular responses such as increases or decreases in cellular proliferation and apoptosis" (Office action of June 23, 2008, page 10, third paragraph). Appellant argues that this language ("determining the functional effect") is no longer present in independent claims 1, 27, or 56. Claim 56 currently recites "assaying the kinase activity of the Axl polypeptide" to identify a compound that inhibits angiogenesis. Healy et al. teach only assaying the effect of Gas 6 on Axl kinase activity. As discussed above, Healy et al. do not teach that Gas 6 is an inhibitor of Axl, when read in fight of Gallicchio et al. Appellant argues that thus, Healy et al. do not expressly or inherently teach the claimed method of identifying a compound that is an inhibitor of angiogenesis and this reference does not anticipate claims 56 or 61.

Appellant's arguments have been considered, but have not been found persuasive because as set forth above, the claims are not limited to using compounds that inhibit angiogensis. Thus, whether or not GAS 6 is an inhibitor of angiogenesis, given that Healy et al. teach assaying the kinase activity of Axl and assaying apoptosis in human endothelial cells expressing recombinant wild type Axl (see Figures 5, 9, and 10) and neither the specification nor claims 56 and 61 limit

how the kinase activity is to be assayed, the teachings of Healy et al. anticipate the methods of claims 56 and 61.

Claim Rejections - 35 USC § 103

Appellant argues that to establish a *prima facie* case of obviousness, the Office must establish that (1) there is some suggestion or motivation to combine the references, either in the references or in common general knowledge of one of skill in the art (MPEP § 2143.01); and (2) there is a reasonable expectation of success (MPEP § 2143.02). In addition, the Office must show that the references teach or suggest all claim limitations. "When determining whether a claim is obvious, an Examiner must make 'a searching comparison of the claimed invention - including all it limitations - with the teaching of the prior art.' Thus, 'obviousness requires a suggestion of all limitations in a claim.'" *Ex parte Mumper* BPAI, Appeal No. 2008-2332, June 27, 2008.

Appellant argues that based on the discussion of Healy et al. above, Appellant argues that Healy et al. do not teach all the limitations of the claims, namely that Healy et al. do not teach or even suggest identification of an inhibitor of angiogenesis. Appellant argues that Healy et al. make no suggestion that Axl polypeptide plays a role in angiogenesis. Appellant argues that rather, Healy et al. teach only that Axl and its ligand Gas 6 have anti-apoptotic activity in HPAEC cells and that this may be "relevant to endothelial cell survival in the quiescent environment of the vessel wall" (Healy et al., abstract).

Appellant argues that the Office alleges that Varner and Cheresh teach a role for integrin $\alpha V\beta 3$ in angiogenesis. Appellant argues that however, Varner and Cheresh do not teach or suggest a role for Axl polypeptide in angiogenesis nor selecting a compound that inhibits *in vitro*

kinase activity of Axl polypeptide and inhibits angiogenesis phenotype in a cell-based assay to identify inhibitors of angiogenesis. Appellant argues that therefore, this reference does not cure the deficiencies of Healy et al. Appellant argues that likewise, Panzer et al. and Ruoslahti et al. teach only general methods of screening small molecules and other compounds for use in diagnosis or therapy. Appellant argues that there is no discussion of Axl polypeptide in these references; therefore they cannot cure the deficiencies of Healy et al. Klinghoffer et al. teach only use of siRNAs for altering gene expression. This reference discloses Axl only as containing a potential protein tyrosine phosphatase 1B recognition motif (Klinghoffer et al., paragraph [0016]) and does not teach or suggest a role for Axl polypeptide in angiogenesis. Appellant argues that therefore Klinghoffer et al. cannot be used to cure the deficiencies of Healy et al.

Appellant argues that the Office does not provide any rationale for one of skill in the art to combine or modify the cited references. Taken together, one of skill might be motivated to assay regulation of apoptosis by Axl, but not regulation of angiogenesis. Appellant argues that their claims are based on the novel recognition that inhibition of Axl polypeptide inhibits angiogenesis. None of the cited references disclose that Axl has any role in angiogenesis, nor suggest that inhibitors of Axl could be inhibitors of angiogenesis. Without the recognition that inhibition of Axl inhibits angiogenesis, there is no motivation to combine the references and no expectation of success in arriving at Applicants' claimed invention by combining the references. Appellant argues that thus, alone or in combination, the cited references do not support a primafacie case of obviousness.

Appellant argues that in sum, none of the references cited by the Office teach or suggest, either alone or in combination, all of the features of Applicants' claims. It remains well-settled

law that obviousness requires at least a suggestion of all of the features in a claim. See Ex *parte Mumper* (BPAI, Appeal 2008-2332, June 27, 2008) citing *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) and *In re Royka*, 490 F.2d 981,985 (CCPA 1974). The Office has not met this burden and has not provided any "articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l v. Teleflex*, 127 S. Ct. 1727, 1741 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006).

Appellant's arguments have been considerd, but have not been found persuasive. First, as set forth above, Healy et al. teach the limitations of the process steps claimed in the base claims and the recitation of identifying an inhibitor of angiogenesis in the preamble and the intended result of process steps recited in the wherein claues are not given patentable weight for comparison with the prior art for the reasons set forth above . One of skill in the art would immediately recognize that the study of viability and apoptosis of endothelial cells would be relevant to the study of angiogensis as endothelial cells growth would be required for the formation of additional blood vessels. In particular, Healy et al. state that apoptosis has a role in vascular remodling tumor angiogenesis and a balance between cell growth and death may be required for vascular remodeling, see page L1280- left col. Given the importance of endothelial growth to angiogenesis and vascular remodling and given the importance of these events to normal physiology and disease like tumorigenesis, and given the role shown for Axl activity in endothelial cell survival, one of skill in the art would be motivated to study the effects of various compounds such as an antibody, antisense molecule, RNAi, or small organic molecule taught by Panzer et al., Ruoslahti et al , and Klinghoffer et al. in screens to identify compounds that affect Axl kinase activity and endothelial cell survival. Additionally, given that Varner and Cheresh

teach that integrin αVβ3 is significantly upregulated on vascular cells within human tumors and in response to growth factors and plays a biological role in a critical event of blood vessel formation during tumor angiogenesis, it would be obvious to one of skill in the art to assay the effect that the applied compounds have on αVβ3 expression in conjunction with their effects on Axl kinase activity and cell survival and apoptosis. Thus, for the reasons previously set forth and above, the combined methods would be obvious in view ot the combined teachings of the prior art.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Peter J Reddig/

Examiner, Art Unit 1642

Conferees:

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643

/Gary B. Nickol /

Supervisory Patent Examiner, Art Unit 1646